REMARKS

Claims 1, 7, 10-16, 18-27, 54-56 and 59-63 are pending in the application. Claims 1, 7, 26, 54-56, 60-62 have been objected to. Claims 1, 7, 10-16, 18-27, 54-56 and 59-63 have been rejected. Claims 1, 19, 22, 26-27 and 60 have been amended. Claims 12-16, 54, 57-58 and 61-63 have been cancelled. The amendments to the claims, specification and abstract contain no new matter. Therefore, Applicants respectfully request entry of the Amendment.

PRIORITY

In the office action, the Examiner alleged that the elected subject matter of the current application is not entitled to the April 29, 1999 priority date, the filing date of U.S. patent application No. 09/302,457, since allegedly the human pHyde protein disclosed in the 09/302,457 U.S. application, fails to teach the claimed human pHyde protein of the subject Application. Applicants respectfully disagree.

The Examiner agreed that Figure 19A of U.S. Patent Application Serial Number 09/302,457, filed on April 29, 1999, contains an 856 bp, pHyde gene sequence, referred to in the U.S. Patent Application Serial Number 09/302,457 as SEQ ID NO:5

Applicants maintain that SEQ ID NO:1 of instant invention, should be granted the benefit of the priority date of April 29, 1999, from U.S. Patent Application Serial No. 09/302,457.

An alignment of SEQ ID NO.1 of the instant application, with the human pHyde gene disclosed in SEQ ID NO:5 of U.S. Patent Application Serial Number 09/302457, attached hereto as appendix 2, demonstrate the 733 nucleotide sequence of SEQ ID NO:1 in the current application, which is 100 % contained within the 856 nucleotide sequence of SEQ ID NO: 5 of U.S. Patent Application Serial Number 09/302457.

Amino acid sequence alignments between the translated product SEQ ID NO:5 disclosed in U.S. Patent Application Serial Number 09/302457, and the translated product of the nucleotide SEQ ID NO:1 of the instant application, is attached hereto as appendix 3

demonstrate that the human pHyde amino acid sequence translated from SEQ ID NO:1 share a region of 99% identity with the amino acid sequence translated from SEQ ID NO:5 disclosed in U.S. Patent Application Serial Number 09/302457. SEQ ID NO 1 of the current application shares 98% identity with the nucleotide SEQ ID NO:5 disclosed in U.S. Patent Application Serial Number 09/302457. Applicants maintain that the greater than 98 % identity between the nucleotide sequences of the April 29, 1999 U.S Patent Application Serial Number 09/302457 and the instant application, provides sufficient support for the claimed sequences of the instant invention, and should be granted a priority date of April 29, 1999.

COMPLIANCE WITH THE SEQUENCE RULES

In the Office Action, the Examiner noted that SEQ ID NO:7,, the direct translated product of SEQ ID NO:3, was not filed. The Examiner indicated that the sequence would not be considered new matter. In response, Applicants are providing a new sequence listing, which discloses SEQ ID NO:7 . Accordingly Applicants respectfully request entry of the sequence listing.

OBJECTIONS

In the Office Action, the Examiner objected to the specification as containing confusing reference material. In response, Applicants have amended the specification to remove the material in question. Accordingly, Applicants respectfully request that the Examiner withdraw the objection.

In the Office Action, the Examiner objected to the Abstract as allegedly failing to completely describing the disclosed subject matter. In response, Applicants have amended the abstract as suggested by the Examiner to refer to both human and rat pHyde proteins. Accordingly, Applicants respectfully request that the Examiner withdraw the objection.

In the Office Action, the Examiner objected to the reference to SEQ ID NO:7 on page 83, noting that the sequence listing does not provide such a sequence. In response,

Applicants submit a sequence listing disclosing SEQ ID NO: 7, and a statement as required by 37 C.F.R. 1.821 through 1.825 indicating no new matter has been introduced (the Examiner has indicated in the Office Action at sub. 36, that inclusion of the full rat pHyde amino acid sequence which is disclosed in SEQ ID NO: 7 will not constitute new matter). Accordingly, Applicants respectfully request that the Examiner withdraw the objection.

In the Office Action, the Examiner objected to the Claim 1, as having improper language, specifically, the Examiner objected to the use of the phrase "...encoding for...", and suggested amending the claim by changing the phrase to "encodes a protein" In response, Applicants have amended claim 1 as suggested and accordingly, Applicants respectfully request that the Examiner withdraw the objection.

In the Office Action, the Examiner objected to Claims 7, 26 54-56 and 60-62 as improperly depending from claims 1, 25, and 12 respectively, under 37 C.F.R. §175(c). In response, Applicants amended claims 1, 7, 26 55-56 and 60-61 and cancelled claims 25, 12, 54 and 62 in order to correct improper dependency. Accordingly, Applicants respectfully request that the Examiner withdraw the objection.

Applicants thank the examiner for withdrawing the objections to claims 7, 12-17 and 59.

CLAIM REJECTIONS BASED ON 35 U.S.C. § 112 SECOND PARAGRAPH

In the Office Action, the Examiner rejected claims 1, 7, 10-16, 18-27, 54-56 and 59 under 35 U.S.C. § 112 (first paragraph), alleging that disclosure of the partial gene sequence encoding the pHyde protein is insufficient support to enable one skilled in the art to predict the full-length member of the claimed genus. Applicants respectfully disagree.

Applicants have defined the compound structurally. An alignment of the human pHyde nucleotide sequence encoding the pHyde protein with that of the rat (attached hereto as Appendix 3) demonstrate that the human sequence encoding p-Hyde in SEQ ID NO:1

share a region of 84% identity with the full rat sequence encoding pHyde in SEQ ID NO:3 with overall identity of at least 62% for the open reading frame. Additional structural data is disclosed on page 83, lines 25-29, noting average hydrophilicity between specific residues. Thus, the human pHyde protein has been defined structurally.

Applicants have also defined a human pHyde protein and a nucleic acid encoding the same, functionally. Both the human and Rat pHyde proteins disclosed, are regulated the same way, as evident from the differential expression of both rat and human *pHyde,* in prostate cancer cell lines (page 82, lines 23-25, page 86, lines 30-34). One skilled in the art would necessarily agree that a molecule whose partial encoding sequence shares a region of more than 84% identity with a sequence encoding the index protein, and whose expression is regulated the same way belongs to the same family, and is thus defined. One skilled in the art would have necessarily appreciated, at the time of the invention, that a human pHyde molecule was described adequately, given the state of the art, the shared identity with the rat protein, and the fact that the two are related structurally and functionally.

Further, the specification gives considerable direction and guidance (Examples 1-2) on the use of pHyde in inducing cell susceptibility to apoptosis and in tumor suppression. A high level of skill in the art existed at the time the application was filed, with the methods needed to practice the invention being well known. Moreover, working examples were provided in the specification (see e.g. *In re Wands,* 858 F.2d at 736-40, 8 USPQ2d at 1403-07).

In view of the degree of shared identity between the partial human sequence and the full rat sequence, the differential expression in prostate cancer cells, the degree of skill in the relevant art, the existence of working examples and the fact that all methods for practicing the invention were well known at the time the application was filed, Applicants submit that sufficient support exists for claims directed to a human pHyde protein, and nucleic acids encoding the same, enabling one skilled in the art to predict the members of the claimed genus. Accordingly, Applicants request that the 112 rejection of claims 1, 7, 10-11, 16, 18-27, 54-56 and 59, be withdrawn.

In the office action the Examiner rejected claims 60-63 under 35 U.S.C. § 112 (first paragraph). Specifically, the examiner alleges that disclosure of the partial gene encoding pHyde protein (the genus member) in SEQ ID NO:1 was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of mutants, variants or analogs of the sequences claimed. Applicants respectfully disagree, however, in the interest of expediting prosecution, have cancelled claims 61-63 and amended claim 60 to recite an isolated nucleic acid, encoding an amino acid sequence comprising the sequence as set for the in SEQ ID NO. 2. Applicants submit that support for claim 60 exists, and directs the Examiner's attention to the arguments set forth herein for support for claim 1, which is similar in scope to claim 60. Accordingly, Applicants request withdrawal of the rejection of claims 60-63.

In the Office Action, the Examiner rejected claim 16 under 35 U.S.C. § 112 (second paragraph), as being indefinite for the phrase "sequence complimentary to" in the body of the claim. In response Applicants cancelled claim 16, rendering the rejection moot. Accordingly Applicants respectfully request that the Examiner withdraw the rejection.

In the Office Action, the Examiner rejected claim 22 under 35 U.S.C. § 112 (second paragraph), as being indefinite for having an improper antecedent basis. In response, applicants amended claim 22 as suggested by the examiner, to further limit the claim to a replication-deficient adenovirus type 5 expression vector. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

In the Office Action, the Examiner rejected claims 61 and 63 under 35 U.S.C. § 112 (second paragraph), for use of the term "analog", which the Examiner alleges is unclear as to its metes and bounds. In response, Applicants cancelled claims 61 and 63, rendering the rejection moot. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

35 U.S.C. § 102 Rejections

In the Office Action, the Examiner rejected claims 12-15 and 62-63,under 35 U.S.C. § 102(b) as being anticipated by Hillier et al. and Talerman et al. In response, Applicants cancelled claims 12-15 and 62-63, rendering the rejection moot. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

In the Office Action, the Examiner rejected claims 12-15, 54,55 and 61-63 under 35 U.S.C. § 102(e) as being anticipated by Ni et al. (USPAP 2002/0064818). In response, Applicants cancelled claims 12-15, 54 and 61-63, rendering the rejection of these claims moot. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

Applicants amended claims 55, however, to recite " An isolated nucleic acid molecule comprising a nucleic acid sequence which shares at least 85% identity with the nucleic acid sequence of SEQ ID NO: 1".

Ni was alleged to be an anticipating reference because the sequence listed as SEQ ID NO: 17 describes a 1038 bp nucleotide fragment, which shares roughly 90 % identity with a claimed nucleic acid of the instant invention (SEQ ID NO:1).

Applicants disagree. Applicants maintain that the instant invention should be awarded the priority date of, April 29, 1999, as described above, which antedates the September 3, 1999 priority date of Ni et al, and therefore Ni is not an appropriate reference in this context.

As described above, SEQ ID NO: 1 shares 98.7% identity with the human pHyde nucleotide sequence disclosed in U.S Patent Application Serial Number 09/302,457, filed April 29, 1999, and accordingly should be granted the benefit of priority therefrom.

Accordingly, Applicants respectfully request withdrawal of the rejection.

CLAIM REJECTIONS BASED ON 35 U.S.C. § 101

In the office action, In the Office Action, the Examiner rejected claims 1, 7, 10-16, 18-27, 54-56 and 59-60 under 35 U.S.C. § 101 for allegedly lacking patentable utility. Specifically, the examiner alleged that disclosure of the partial gene encoding pHyde protein (the genus member) in SEQ ID NO:1 is insufficient support for claims directed to functionality of the human pHyde. Applicants respectfully disagree.

With regards to the asserted utility (page 2, line 33; page 3, line 7), the MPEP notes that in determining utility, the Examiner must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion.

The Examiner does not dispute that a pHyde protein, broadly, has utility. The Examiner has instead alleged that a partial human p-Hyde protein will not have the same utility as a full length protein. Applicants disagree with the allegation that the instant invention is only regarding a partial protein.

Applicants have defined the claimed pHyde protein. Applicants have defined the protein structurally, in providing: a human pHyde nucleotide sequence as set forth in SEQ ID NO:1, which shares a region of 84% identity with the rat nucleotide sequence (SEQ ID NO:3), which encodes a full length rat pHyde protein. Additional structural data is provided in terms of the average hydrophilicity between specific residues, (page 83, lines 25-29).

Applicants have also defined a pHyde protein and nucleotide sequence encoding the same, functionally. Differential expression of both rat and human *pHyde* was evident in prostate cancer cell lines, suggesting a functional correlation between *pHyde* expression and prostate cancer progression (page 82, lines 23-25, page 86, lines 30-34).

Applicants maintain that a human p-Hyde protein is described in the instant invention, and that the invention is not only a partial protein. Applicants also maintain that the partial human a sequence, the shared identity of that segment with the full rat, evidence that the human gene encoding the protein is regulated comparably to the rat, all provide sufficient support for the claimed human pHyde, and assert its utility. The MPEP at Chapter 2100, section 2163 notes that determination of the existence of sufficient evidence of possession by the inventors, of a chemical species, include the level of skill and knowledge in the art, disclosure of partial structure, physical and/or chemical properties, functional characteristics, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species, is sufficient. (See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406).

As discussed above the specification discloses differential expression of *pHyde* protein in both Dunning rat and human prostate cancer cell lines, indicating their comparable regulation, ergo a functional correlation. A role for pHyde in tumor suppression and promotion of apoptosis is demonstrated as well, thus the utility of a pHyde protein is well supported in the instant invention.

In view of the degree of shared identity, comparable regulation, the indicated function, the degree of skill in the relevant art, the existence of working examples and the fact that all methods for practicing the invention were well known at the time the application was filed, Applicants submit that sufficient support exists for claims directed to full human pHyde gene, and demonstrating a clear utility for a human pHyde protein. Accordingly, Applicants request that the 35 U.S.C. § 101 rejection of claims 1, 7, 10-16, 18-27, 54-56 and 59-60, be withdrawn.

INVENTORSHIP

Applicants assert that Chiang Wang was not associated with the subject matter claimed in the current application.

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 05-0649.

Respectfully submitted,

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Dated: September 21, 2005

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